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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/614,333	07/03/2003	R. Rogers Yocum	BGI-154B	5952
959	7590	10/23/2006	EXAMINER	
LAHIVE & COCKFIELD, LLP ONE POST OFFICE SQUARE BOSTON, MA 02109-2127			FRONDA, CHRISTIAN L	
			ART UNIT	PAPER NUMBER
			1652	

DATE MAILED: 10/23/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/614,333

Applicant(s)

YOCUM ET AL.

Examiner

Christian L. Fronda

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 11 September 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-28,30-33,42,43 and 46-51 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-28,30-33,42,43 and 46-51 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 03 July 2003 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date 10/05/05.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____.

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DETAILED ACTION

1. Applicant's election with traverse of Group I, encompassing amended claims 1-22, 42, 43, 46-49, 50, and 51, in the reply filed on 09/11/2006 is acknowledged. In view of applicants extensive claims amendments filed 09/11/2006, the previous restriction requirement has been withdrawn. Claims 23-28 and 30-33 will also be examined.
2. Claims 1-28, 30-33, 42, 43, 46-51 are pending and under consideration in this Office Action.

Claim Rejections - 35 U.S.C. § 112, 2nd Paragraph

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.
4. Claims 1-28, 30-33, 42, 43, 46-51 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.
The claims recite the phrase "pantothenate production is enhanced" which is relative term that is vague and indefinite. It is not clear to what degree of enhancement of pantothenate production is encompassed by the phrase. Dependent claims 3-28, 30-33, 42, 43, 46-51 are also rejected because they do not correct this defect.
Amending the claims to recite that pantothenate production by the transformed microorganism is increased compared to an unmodified microorganism may overcome the rejection.
Furthermore, claims 25 -27 is directed toward down regulating or deleting "CoaA" and/or "CoaX" which renders the claim vague and indefinite since it is not clear if applicants are actually referring to the genes encoding these gene products are actually down regulated or deleted.

Claim Rejections - 35 U.S.C. § 112, 1st Paragraph

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:
The specification shall contain a written description of the invention, and of the manner and

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process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1-33, 42, 43, 46-51 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are genus claims that are directed toward process for producing pantothenate using a genus of microorganisms having any deregulation of any enzyme/protein in methylenetetrahydrofolate (MTF) biosynthetic pathway (including any GlyA gene product, SerA gene product, and PurR gene product), any deregulation of any enzyme/protein in the pantothenate biosynthetic pathway (including any ketopantoate hydroxymethyltransferase, ketopantoate reductase, pantothenate synthetase, aspartate decarboxylase, pantothenate kinase), any/or deregulation of any isoleucine-valine biosynthetic pathway (including any acetohydroxyacid synthetase, acetohydroxyacid isomeroreductase, and dihydroxyacid dehydratase).

The scope of the genus includes many members with widely differing structural, chemical, and physiochemical properties including widely differing amino acid/nucleotide sequences and biological functions for the protein/enzymes in the recited biosynthetic pathways. Furthermore, each genus is highly variable because a significant number of structural and biological differences between genus members exist.

For claims drawn to a genus, MPEP § 2163 states the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show that applicant was in possession of the claimed genus. See *Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1406. MPEP § 2163 states that a representative number of species means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus.

Example III of the specification discloses a plasmid pAN396 (SEQ ID NO: 24) transformed into a *Bacillus subtilis* strain resulting in the transformed *B. subtilis* producing more pantothenate compared to an untransformed *B. subtilis* strain, where the said plasmid contains a *B. subtilis* polynucleotide encoding a serine hydroxymethyl transferase (GlyA gene product)

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obtained using primers of SEQ ID NOs: 22 and 23. Example IV discloses a plasmid pAN393 (SEQ ID NO: 25) transformed into a *B. subtilis* strain resulting in the transformed *B. subtilis* producing more pantothenate compared to an untransformed *B. subtilis* strain, where the said plasmid contains a *B. subtilis* polynucleotide encoding a 3-phosphoglycerate dehydrogenase (SerA gene product) obtained using primers of SEQ ID NOs: 21 and 22. Example VI discloses plasmid pAN838F (SEQ ID NO: 28) transformed into a *B. subtilis* strain resulting in the transformed *B. subtilis* having a disrupted repressor protein (PurR gene product) and producing more pantothenate compared to an untransformed *B. subtilis* strain, where the said plasmid contains a disrupted *B. subtilis* polynucleotide encoding the repressor protein PurR. Example VII discloses a plasmid pAN395 (SEQ ID NO: 29) transformed into a *B. subtilis* strain resulting in the transformed *B. subtilis* producing more pantothenate compared to an untransformed *B. subtilis* strain, where the said plasmid contains a *B. subtilis* polynucleotide encoding a 3-phosphoglycerate dehydrogenase (SerA gene product) that is expressed from the strong, constitutive promoter P_{26} .

The specification fails to disclose additional microorganisms which have increased production of pantothenate compared to an untransformed microorganism as encompassed by the claimed genus, which are widely variant in their physiological characteristics, functions, and/or structures. As such the disclosure of the above mentioned microorganisms of the claimed genus is insufficient to be representative of the attributes and features common to all the members of the claimed genus. Thus, one skilled in the art cannot visualize or recognize the identity of the members of the genus. Furthermore, the recitation names such as "MTF biosynthetic pathway", "pantothenate biosynthetic pathway", and "isoleucine-valine biosynthetic pathway" does not define any structural features and amino acid/nucleotides sequences commonly possessed by the enzyme/proteins of the claimed genus.

The Court of Appeals for the Federal Circuit has recently held that a "written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definitions, such as the structure, formula [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *University of California v. Eli Lilly and Co.* 43 USPQ2d 1398 (Fed. Cir. 1997), quoting *Fiers v. Revel*, 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) (bracketed material in original). To fully describe the genus of genetic materials, which is a chemical compound, applicants must (1) fully describe at least one species of the claimed genus sufficient to represent said genus whereby a skilled artisan, in view of the prior art, could predict the structure of other species encompassed by the claimed genus and (2) identify the common characteristics of the claimed molecules, e.g. structure, physical and/or chemical characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or a combination of these. Therefore, the instant claims are not adequately described.

In view of the above considerations, one of skill in the art would not recognize that

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applicants were in possession of a process for producing pantothenate using a genus of microorganisms having any deregulation of any enzyme/protein in methylenetetrahydrofolate (MTF) biosynthetic pathway (including any GlyA gene product, SerA gene product, and PurR gene product), any deregulation of any enzyme/protein in the pantothenate biosynthetic pathway (including any ketopantoate hydroxymethyltransferase, ketopantoate reductase, pantothenate synthetase, aspartate decarboxylase, pantothenate kinase), any/or deregulation of any enzyme/protein in the isoleucine-valine biosynthetic pathway (including any acetohydroxyacid synthetase, acetohydroxyacid isomeroreductase, and dihydroxyacid dehydratase)..

Furthermore, a review of the specification indicates that elements which are not particularly described, including regulatory elements, promoters, enhancers, and untranslated regions, are essential to the function of the claimed invention because the claims recite a serA, glyA, panB, panD, purR, coaA, coaX genes. The art indicates that the structure of genes with regulatory elements and untranslated regions is empirically determined. Therefore, the structure of these elements which applicants considers as being essential to the function of the claim are not conventional in the art. There is no known or disclosed correlation between a polynucleotide encoding each of the gene products and the structure of the non-described elements of the recited genes. Furthermore, there is no additional disclosure of physical and/or chemical properties for these non-described elements. In view of the above considerations, one of skill in the art would not recognize that applicants were in possession of the serA, glyA, panB, panD, purR, coaA, coaX genes.

Amending the claims to recite a process for producing pantothenate using a *B. subtilis* strain transformed with a plasmid of SEQ ID NOs: 24, 25, 28 or 29 which over produces pantothenate compared to an untransformed *B. subtilis* strain may overcome the rejection.

7. Claims 1-33, 42, 43, 46-51 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a process for producing pantothenate using a *B. subtilis* strain transformed with a plasmid of SEQ ID NOs: 24, 25, 28 or 29 which over produces pantothenate compared to an untransformed *B. subtilis* strain; does not reasonably provide enablement for any other embodiment as recited in the claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in *re Wands* [858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)]. The Wands factors are: (a) the quantity of experimentation necessary, (b) the amount of direction or guidance presented, (c) the presence or absence of working example, (d) the nature of the invention, (e) the state of the prior art, (f) the relative skill of those in the art, (g) the predictability or unpredictability of the art, and (h) the breadth of the claim.

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The nature and breadth of the claims encompass any process for producing pantothenate using a genus of microorganisms having any deregulation of any enzyme/protein in methylenetetrahydrofolate (MTF) biosynthetic pathway (including any GlyA gene product, SerA gene product, and PurR gene product), any deregulation of any enzyme/protein in the pantothenate biosynthetic pathway (including any ketopantoate hydroxymethyltransferase, ketopantoate reductase, pantothenate synthetase, aspartate decarboxylase, pantothenate kinase), any/or deregulation of any isoleucine-valine biosynthetic pathway (including any acetohydroxyacid synthetase, acetohydroxyacid isomeroreductase, and dihydroxyacid dehydratase).

The specification provides guidance and examples for making the following specific *Bacillus subtilis* strains: Example III of the specification discloses a plasmid pAN396 (SEQ ID NO: 24) transformed into a *B. subtilis* strain resulting in the transformed *B. subtilis* producing more pantothenate compared to an untransformed *B. subtilis* strain, where the said plasmid contains a *B. subtilis* polynucleotide encoding a serine hydroxymethyl transferase (GlyA gene product) obtained using primers of SEQ ID NOs: 22 and 23. Example IV discloses a plasmid pAN393 (SEQ ID NO: 25) transformed into a *B. subtilis* strain resulting in the transformed *B. subtilis* producing more pantothenate compared to an untransformed *B. subtilis* strain, where the said plasmid contains a *B. subtilis* polynucleotide encoding a 3-phosphoglycerate dehydrogenase (SerA gene product) obtained using primers of SEQ ID NOs: 21 and 22. Example VI discloses plasmid pAN838F (SEQ ID NO: 28) transformed into a *B. subtilis* strain resulting in the transformed *B. subtilis* having a disrupted repressor protein (PurR gene product) and producing more pantothenate compared to an untransformed *B. subtilis* strain, where the said plasmid contains a disrupted *B. subtilis* polynucleotide encoding the repressor protein PurR. Example VII discloses a plasmid pAN395 (SEQ ID NO: 29) transformed into a *B. subtilis* strain resulting in the transformed *B. subtilis* producing more pantothenate compared to an untransformed *B. subtilis* strain, where the said plasmid contains a *B. subtilis* polynucleotide encoding a 3-phosphoglycerate dehydrogenase (SerA gene product) that is expressed from the strong, constitutive promoter *P*₂₆.

However, the specification does not provide guidance, prediction, and working for making any other microorganism to be used in the claimed process for producing pantothenate. Thus, an undue amount of trial and error experimentation must be preformed where such experimentation involves making any microorganism having any deregulation of any enzyme/protein in methylenetetrahydrofolate biosynthetic pathway, any deregulation of any enzyme/protein in the pantothenate biosynthetic pathway, any/or deregulation of any enzyme/protein in the isoleucine-valine biosynthetic pathway; and determining whether the microorganism can overproduce pantothenate compared to an unmodified microorganism. This trial and error experimentation is well outside the scope of routine experimentation. General teaching regarding screening and searching for a specific microorganism that overproduces

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pantothenate compared to an unmodified microorganism is not guidance for making the claimed invention. In view of the above considerations, the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Amending the claims to recite a process for producing pantothenate using a *B. subtilis* strain transformed with a plasmid of SEQ ID NOs: 24, 25, 28 or 29 which over produces pantothenate compared to an untransformed *B. subtilis* strain may overcome the rejection.

Conclusion

8. No claims are allowed.
9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christian L Fronda whose telephone number is (571)272-0929. The examiner can normally be reached Monday-Friday between 9:00AM - 5:00PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura N Achutamurthy can be reached on (571)272-0928. The fax phone number for the organization where this application or proceeding is assigned is (571)273-8300.
10. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

CLF


TEKCHAND SAIDHA
PRIMARY EXAMINER